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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Platzek, et al.

Group Art Unit: TBA

Serial No.: 09/925,618

Examiner: TBA

Filed: August 10, 2001

For: USE OF PERFLUOROALKYL-CONTAINING METAL COMPLEXES AS  
CONTRAST MEDIA IN MR-IMAGING FOR VISUALIZATION OF PLAQUE,  
TUMORS AND NECROSES

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

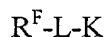
**IN THE CLAIMS:**

Please amend the claims as follows:

3. (Amended) Use according to claim 1, wherein the metal complexes are also used as MRI contrast media for visualization of infarcted and necrotic tissue.

4. (Amended) Use according to claim 1, wherein the metal complexes are also used as MRI contrast media for independent visualization of necroses and tumors.

8. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula I



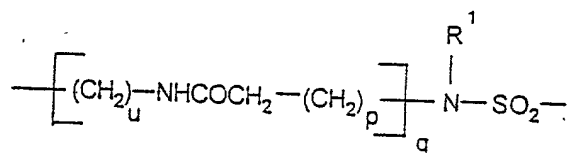
I

in which

$R^F$  is a perfluorinated, straight-chain or branched carbon chain with formula  $-C_nF_{2n}E$ , in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom  
and n stands for numbers 4-30,

L means a direct bond, a methylene group, an -NHCO group, a group



whereby p means the numbers 0 to 10, and q and n, independently of one another, mean numbers 0 or 1, and

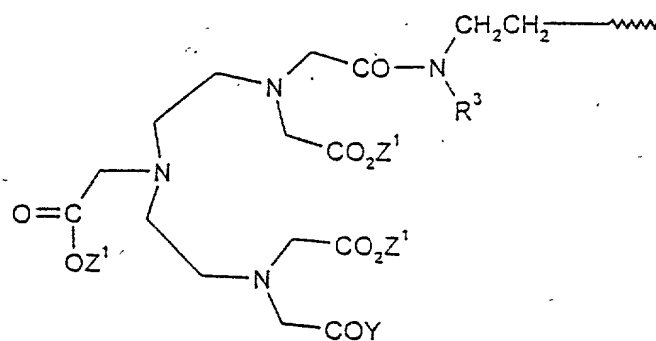
R<sup>3</sup> is a hydrogen atom, a methyl group, a -CH<sub>2</sub>-OH group, a -CH<sub>2</sub>-CO<sub>2</sub>H group or a C<sub>2</sub>-C<sub>15</sub> chain, which optionally is interrupted by 1 to 3 oxygen atoms, 1 to 2 >CO groups or an optionally substituted aryl group and/or is substituted with 1 to 4 hydroxyl groups, 1 to 2 C<sub>1</sub>-C<sub>4</sub> alkoxy groups, 1 to 2 carboxy groups, a group -SO<sub>3</sub>H-,

or is a straight-chain, branched, saturated or unsaturated C<sub>2</sub>-C<sub>30</sub> carbon chain, which optionally contains 1 to 10 oxygen atoms, 1 to 3 -NR<sup>a</sup> groups, 1 to 2 sulfur atoms, a piperazine, a -CONR<sup>a</sup> group, an -NR<sup>a</sup>CO group, an -SO<sub>2</sub> group, an -NR<sup>a</sup>-CO<sub>2</sub> group, 1 to 2 CO groups, a group -CO-N-T-N(R<sup>a</sup>)-SO<sub>2</sub>-R<sup>F</sup>, or 1 to 2 optionally substituted aryls and/or is interrupted by these groups and/or is optionally substituted with 1 to 3 -OR<sup>a</sup> groups, 1 to 2 oxo groups, 1 to 2 -NH-COR<sup>a</sup> groups, 1 to 2 -CONHR<sup>a</sup> groups, 1 to 2 -(CH<sub>2</sub>)<sub>p</sub>-CO<sub>2</sub>H groups, 1 to 2 groups -(CH<sub>2</sub>)<sub>p</sub>-(O)<sub>q</sub>-CH<sub>2</sub>CH<sub>2</sub>-R<sup>F</sup>, whereby

R<sup>a</sup>, R<sup>F</sup> and p and q have the above-indicated meanings, and

T means a C<sub>2</sub>-C<sub>10</sub> chain, which optionally is interrupted by 1 to 2 oxygen atoms or 1 to 2 -NHCO groups,

K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides, specifically for a complexing agent or complex of general formula II



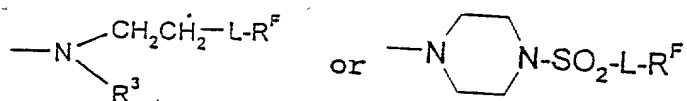
(II)

in which  $R^c$ ,  $R^1$  and B are independent of one another, and

$R^c$  has the meaning of  $R^a$  or means  $-(CH_2)_m-L-R^F$ , whereby m is 0, 1 or 2, and L and  $R^F$  have the above-mentioned meaning,

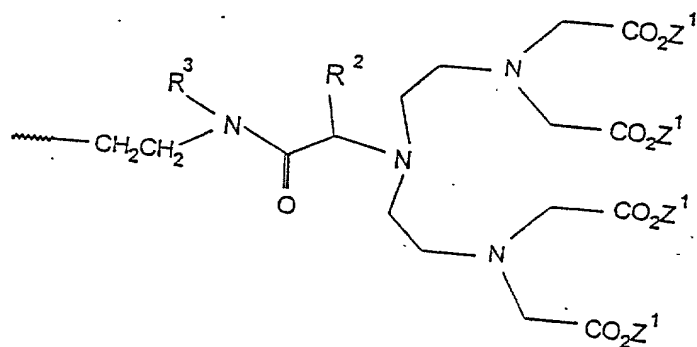
$R^1$ , independently of one another, mean a hydrogen atom or a metal ion equivalent of atomic numbers 22-29, 42-46 or 58-70,

B means  $-OR^1$  or



whereby  $R^1$ , L,  $R^F$  and  $R^c$  have the above-mentioned meanings, or

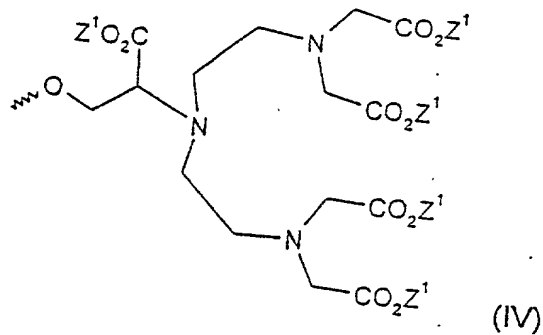
K stands for a complexing agent or complex of general formula III



(III)

in which  $R^c$  and  $R^1$  have the above-mentioned meanings and  $R^b$  has the meaning of  $R^a$   
or

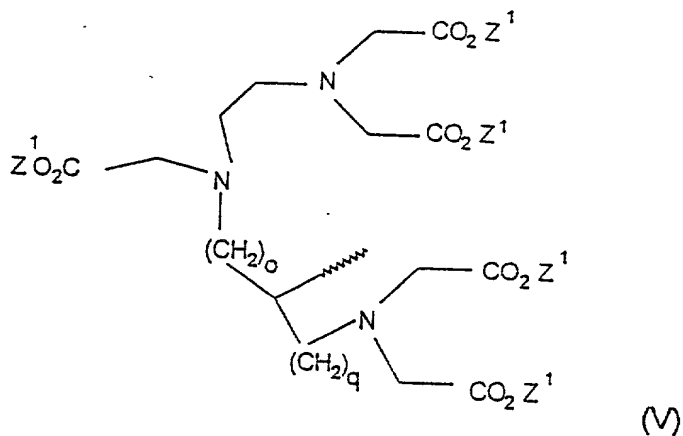
K stands for a complexing agent or complex of general formula IV



in which  $R^1$  has the above-mentioned meaning

or

K stands for a complexing agent or complex of general formula V

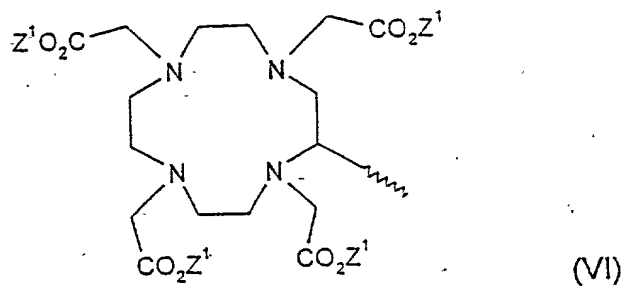


in which  $R^1$  has the above-mentioned meaning, and o and q stand for numbers 0 or 1,

and yields the sum  $o + q = 1$ ,

or

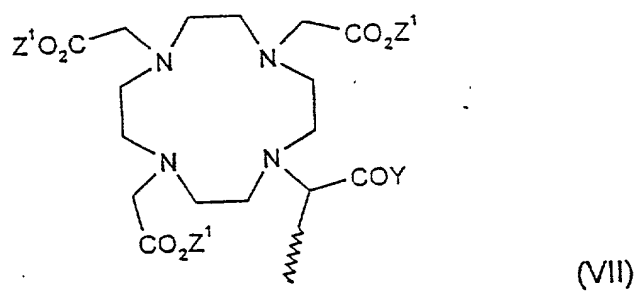
K stands for a complexing agent or complex of general formula VI



in which  $R^1$  has the above-mentioned meaning

or

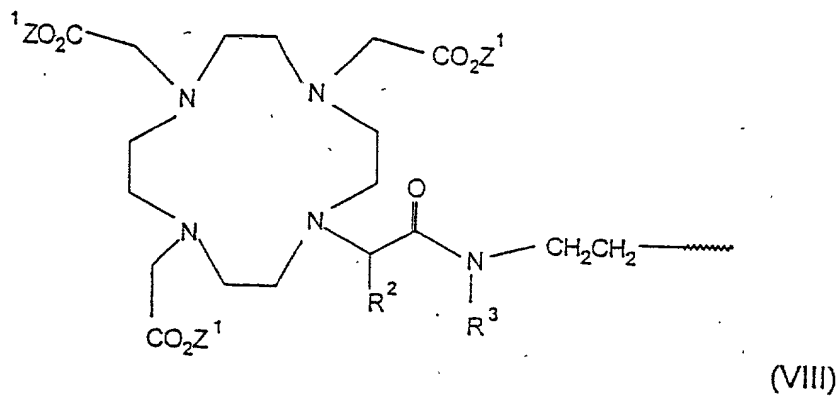
K stands for a complexing agent or complex of general formula VII



in which  $R^1$  and B have the above-mentioned meanings

or

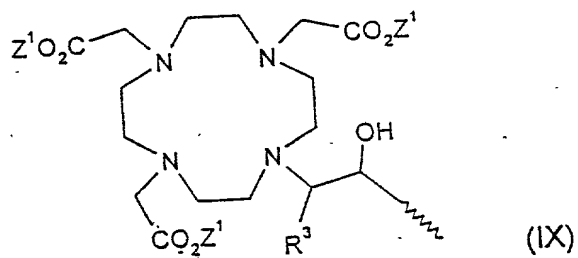
K stands for a complexing agent or complex of general formula VIII



in which  $R^c$  and  $R^1$  have the above-mentioned meanings, and  $R^b$  has the above-mentioned meaning of  $R^a$

or

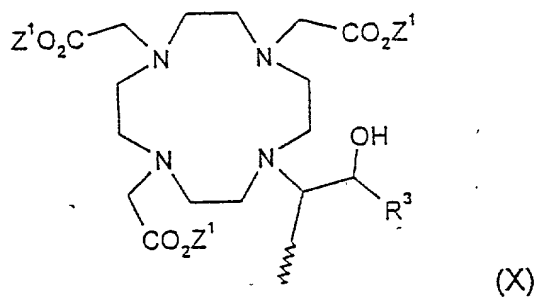
K stands for a complexing agent or complex of general formula IX



in which  $R^c$  and  $R^1$  have the above-mentioned meanings,

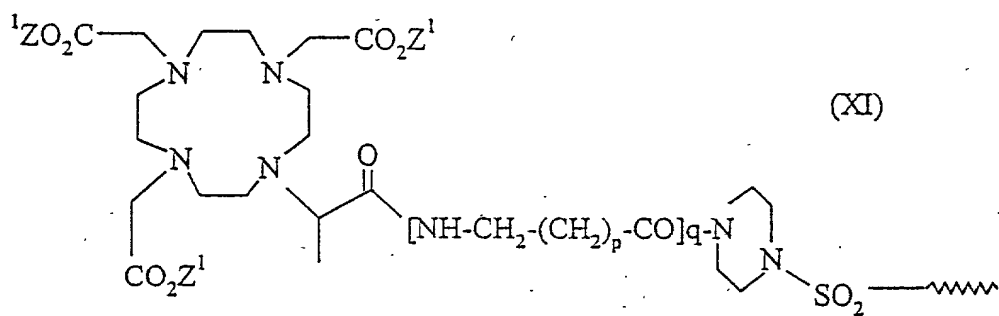
or

K stands for a complexing agent or complex of general formula X



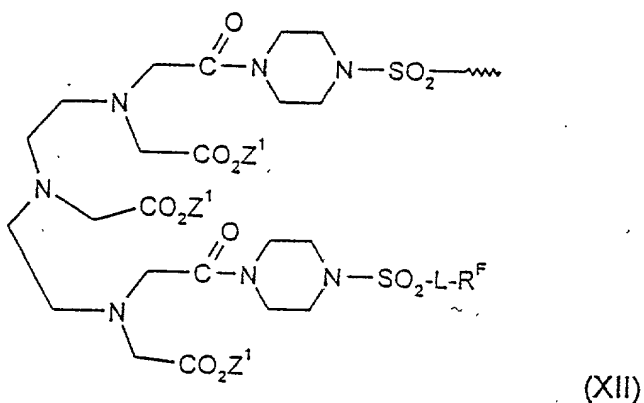
in which R<sup>a</sup> and R<sup>i</sup> have the above-mentioned meanings,  
or

K stands for a complexing agent or complex of general formula XI



in which R<sup>i</sup>, p and q have the above-mentioned meanings, and R<sup>b</sup> has the meaning of R<sup>a</sup>,  
or

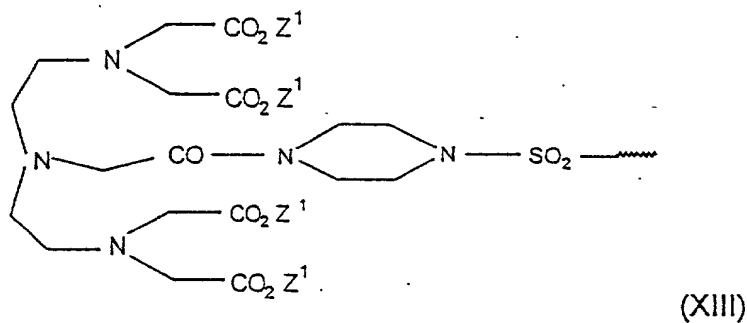
K stands for a complexing agent or complex of general formula XII



in which L, R<sup>F</sup> and Z<sup>1</sup> have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XIII



in which R<sup>1</sup> has the above-mentioned meaning, are used.

10 (Amended) Use according to claim 8, wherein the compounds of formula I in which n in formula -C<sub>n</sub>F<sub>2n</sub>E stands for numbers 4-15 and/or E in this formula means a fluorine atom are used.

11. (Amended) Use according to claim 8, wherein the following compounds are used:



- Gadolinium complex of 10-[1-methyl-2-oxo-3-aza-5-oxo-{4-perfluorooctylsulfonyl-piperazin-1-yl}-pentyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17-heptafluoroheptadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5,9-dioxo-9-{4-perfluorooctyl}-piperazin-1-yl}-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-oxa-1H,1H,2H,3H,3H,5H,5H,6H,6H-perfluorotetradecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,-16,16,17,17,18,18,19,19-henicosafuoro-nonadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-11-aza-11-(perfluorooctylsulfonyl)-tridecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-8-phenyl-octyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraaza-cyclododecane.

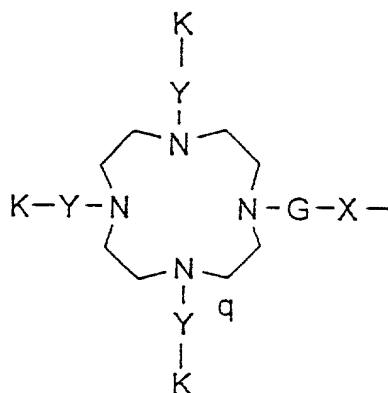
12. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ia



in which

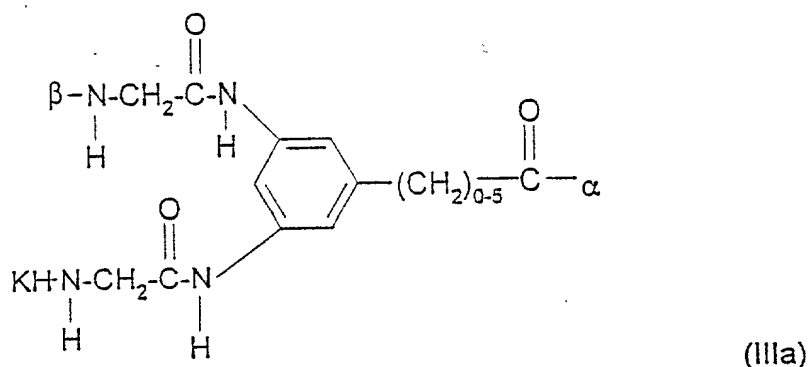
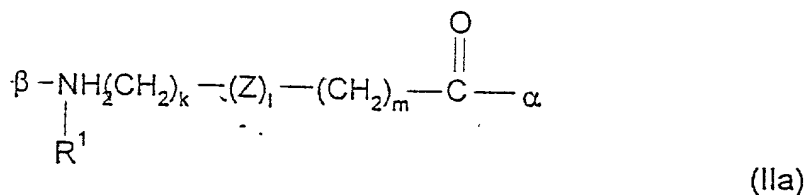
- A is a molecule part that contains 2 to 6 metal complexes, which are bonded directly or via a linker to a nitrogen atom of an annular skeleton chain, and
- $R^F$  is a perfluorinated, straight-chain or branched carbon chain with formula - $C_nF_{2n}E$ , in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom,  
and n stands for numbers 4-30,  
whereby molecule part A has the following structure:



whereby

- $q^1$  is a number 0, 1, 2 or 3,
- K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides,
- X is a direct bond to the perfluoroalkyl group, a phenylene group or a  $C_1$ - $C_{10}$  alkylene chain, which optionally contains 1-15 oxygen atoms, 1-5 sulfur atoms, 1-10 carbonyl groups, 10-10 ( $NR^d$ ) groups, 1-2  $NR^dSO_2$  groups, 1-10  $CONR^d$  groups, 1 piperidine group, 1-3  $SO_2$  groups and 1-2 phenylene groups or optionally is substituted by 1-3 radicals  $R^F$ , in which  $R^d$  stands for a hydrogen atom, a phenyl group, benzyl group or a  $C_1$ - $C_{15}$  alkyl group, which optionally contains 1-2  $NHCO$ , 1-2  $CO$  groups, 1-5 oxygen atoms and optionally is substituted by 1-5 Hydroxy, 1-5 methoxy, 1-3 carboxy, or 1-3  $R^F$  radicals,
- V is a direct bond or a chain of general formula IIa or IIIa:



in which

- $\text{R}^{\circ}$  is a hydrogen atom, a phenyl group, a benzyl group or a  $\text{C}_1\text{-C}_7$  alkyl group, which optionally is substituted with a carboxy group, a methoxy group or a hydroxy group,
- $\text{W}$  is a direct bond, a polyglycol ether group with up to 5 glycol units, or a molecule part of general formula IVa



in which  $\text{R}^h$  is a  $\text{C}_1\text{-C}_7$  carboxylic acid, a phenyl group, a benzyl group or a  $-(\text{CH}_2)_{1-5}$ -

NH-K group,

- $\alpha$  represents the binding to the nitrogen atom of the skeleton chain,  $\beta$  represents the binding to complexing agents or metal complex K,
- and in which variables  $k$  and  $m$  stand for natural numbers between 0 and 10, and  $l$  stands for 0 or 1

and whereby

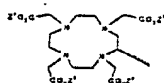
- $\text{D}$  is a CO or  $\text{SO}_2$  group, are used.

20. (Amended) Use according to claim 12, wherein the compounds of general formula Ia in which the perfluoroalkyl chain is  $\text{R}^{\text{F}} - \text{C}_6\text{F}_{13}$ ,  $-\text{C}_8\text{F}_{17}$ ,  $-\text{C}_{10}\text{F}_{21}$  or  $-\text{C}_{12}\text{F}_{25}$  are used.

21. (Amended) Use according to claim 12, wherein the gadolinium complex of 1,4,7-

tris{1,4,7-tris(N-(carboxylatomethyl)-10-[N-1-methyl-3,6-diaza-2,5,8-trioxooctane-1,8-diyl]-1,4,7,10-tetraazacyclododecane, Gd complex}-10-[N-2H,2H,4H,4H,5H,5H-3-oxa-perfluorotridecanoyl]-1,4,7,10-tetraazacyclododecane is used.

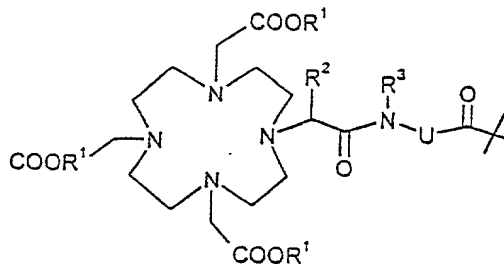
22. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ib



(Ib)

in which

K means a complexing agent or a metal complex of general formula IIb



(IIb)

whereby

$R^1$  stands for a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70,

$R^2$  and  $R^3$  stand for a hydrogen atom, a  $C_1$ - $C_7$  alkyl group, a benzyl group, a phenyl group,  $-CH_2OH$  or  $-CH_2-OCH_3$ ,

U<sup>2</sup> stands for radical L<sup>1</sup>, whereby L<sup>1</sup> and U<sup>2</sup>, independently of one another, can be the same or different,

A<sup>1</sup> means a hydrogen atom, a straight-chain or branched C<sub>1</sub>-C<sub>30</sub> alkyl group, which optionally is interrupted by 1-15 oxygen atoms, and/or optionally is substituted with 1-10 hydroxy groups, 1-2 COOH groups, a phenyl group, a benzyl group and/or 1-5 -OR<sup>9</sup> groups, with R<sup>9</sup> in the meaning of a hydrogen atom or a C<sub>1</sub>-C<sub>7</sub> alkyl radical, or -L<sup>1</sup>-R<sup>F</sup>,

L<sup>1</sup> means a straight-chain or branched C<sub>1</sub>-C<sub>30</sub> alkylene group, which optionally is interrupted by 1-10 oxygen atoms, 1-5 -NH-CO groups, 1-5 -CO-NH groups, by a phenylene group optionally substituted by a COOH- group, 1-3 sulfur atoms, 1-2 -N(B<sup>1</sup>)-SO<sub>2</sub> groups and/or 1-2 -SO<sub>2</sub>-N(B<sup>1</sup>)-groups with B<sup>1</sup> in the meaning of A<sup>1</sup>, an NHCO group, a CONH group, an N(B<sup>1</sup>)-SO<sub>2</sub> group or an -SO<sub>2</sub>-N(B<sup>1</sup>) group and/or optionally is substituted with radical R<sup>F</sup>, and

R<sup>F</sup> means a straight-chain or branched perfluorinated alkyl radical of formula C<sub>n</sub>F<sub>2n</sub>E, whereby n stands for number 4-30, and

E stands for a terminal fluorine atom, chlorine atom, bromine atom, iodine atom or a hydrogen atom,

and optionally present acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides, are used.

29. (Amended) Use according to claim 22, wherein the following compounds are used:
- 1,4,7-Tris(carboxylatomethyl)-10-(3-aza-4-oxo-hexan-5-yl)-acid-(2,3-dihydroxypropyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide]-1,4,7,10-tetraazacyclododecane, gadolinium complex
  - 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-yl)-acid-N-(3,6,9,12,15-pentaoxa)-hexadecyl]-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide]-1,4,7,10-tetraazacyclododecane, gadolinium complex
  - 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-yl)-acid-N-5-hydroxy-3-oxa-pentyl]-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide]-

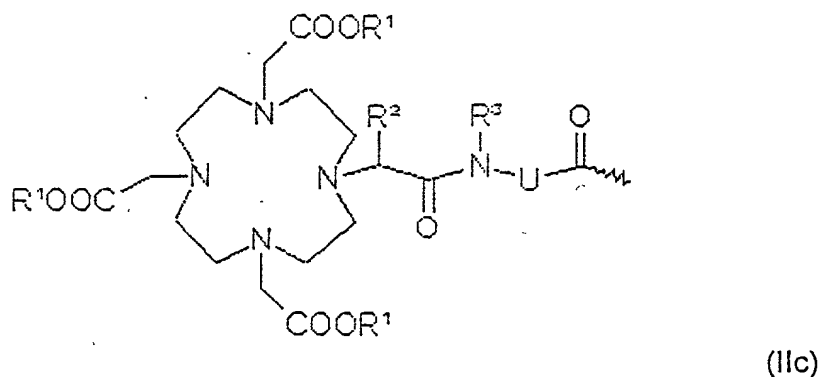
- 1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-{(3-aza-4-oxo-hexan-5-ylidene)-acid-[N-3,6,9,15-tetraoxa-12-aza-15-oxo-C<sub>17</sub>-C<sub>26</sub>-hepta-decafluor)hexacosyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-ylidene)-acid-N-(2-methoxyethyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex.

30. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, the compounds with sugar radicals of general formula Ic



in which

- R represents a mono-or oligosaccharide radical bonded by the 1-OH- or 1-SH-position,
- R<sup>F</sup> is a perfluorinated, straight-chain or branched carbon chain with the formula -C<sub>n</sub>F<sub>2n</sub>E, in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,
- K stands for a metal complex of general formula IIc,



in which

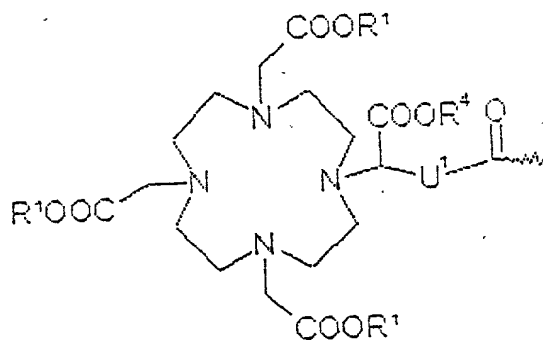
$R^1$  means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two  $R^1$  stand for metal ion equivalents,

$R^2$  and  $R^3$ , independently of one another, represent hydrogen,  $C_1$ - $C_7$  alkyl, benzyl, phenyl,  $-CH_2OH$  or  $-CH_2OCH_3$ , and

$U$  represents  $-C_6H_4-O-CH_2-\omega$ ,  $-(CH_2)_{1-5}-\omega$ , a phenylene group,  $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega$ ,  $-C_6H_4-(OCH_2CH_2)_{0-1}-N(CH_2COOH)-CH_2-\omega$ , or a  $C_1$ - $C_{12}$  alkylene group or  $C_7$ - $C_{12}$ - $C_6H_4-O$  group optionally interrupted by one or more oxygen atoms, 1 to 3  $-NHCO$  groups or 1 to 3  $-CONH$  groups and/or substituted with 1 to 3  $-(CH_2)_{0-5} COOH$  groups, whereby  $\omega$  stands for the binding site to  $-CO-$ ,

or

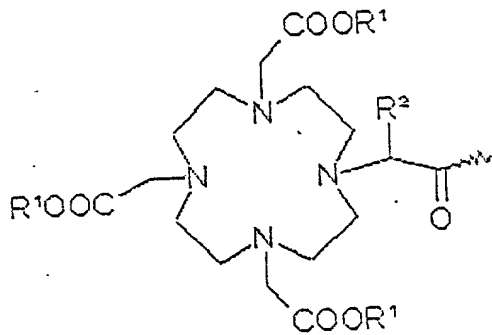
of general formula IIIc



(IIIc)

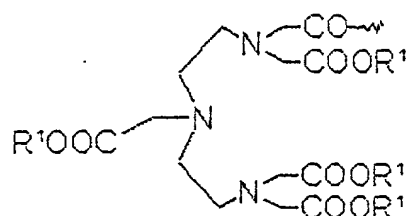
in which  $R^1$  has the above-mentioned meaning,  $R^4$  represents hydrogen or a metal ion equivalent mentioned under  $R^1$ , and  $U^1$  represents  $-C_6H_4-O-CH_2-\omega$ , whereby  $\omega$  means the binding site to  $-CO-$ ,

or of general formula IVc

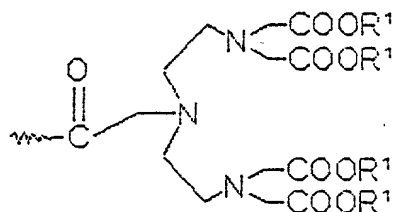


(IVc)

in which  $R^1$  and  $R^2$  have the above-mentioned meaning or of general formula VcA or VcB

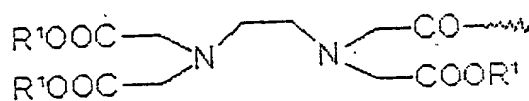


(VcA)



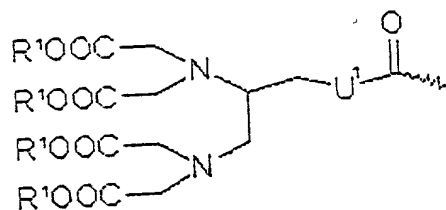
(VcB)

in which  $R^1$  has the above-mentioned meaning, or of general formula VIc



(VIc)

in which  $R^1$  has the above-mentioned meaning, or of general formula VIlc

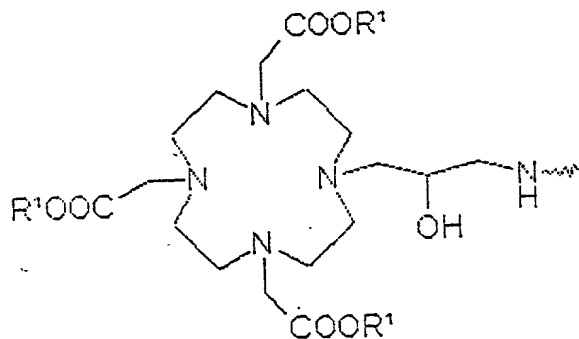


(VIlc)



in which  $R^1$  has the above-mentioned meaning, and

$U^1$  represents  $-C_6H_4-O-CH_2-\omega$ , whereby  $\omega$  means the binding site to  $-CO-$  or of general formula VIIIc



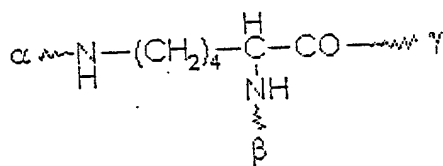
(VIIIc)

in which  $R^1$  has the above-mentioned meaning,

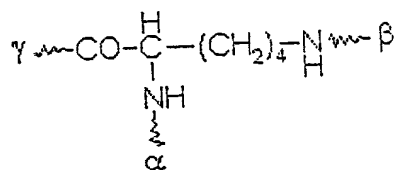
and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

G for the case that K means metal complexes IIc to VIIc represents a radical that is functionalized in at least three places and is selected from the following radicals a) to j)

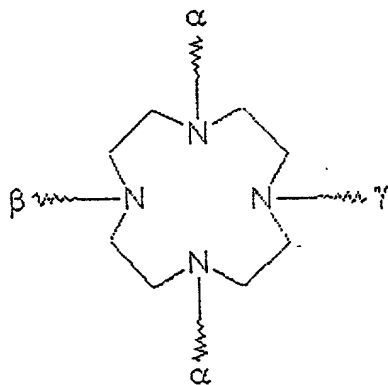
(a)



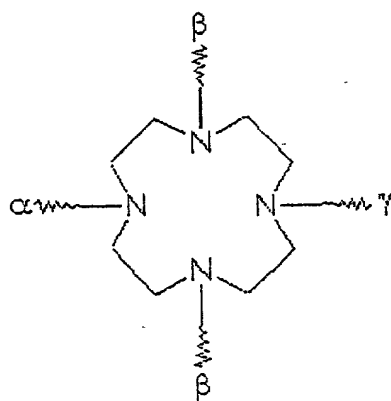
(b)



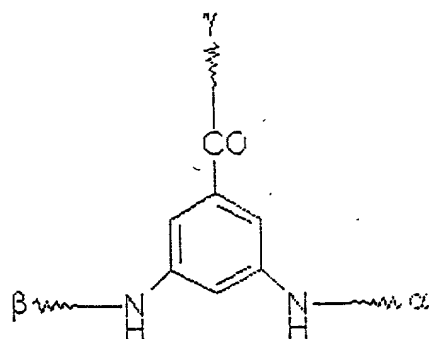
(C)



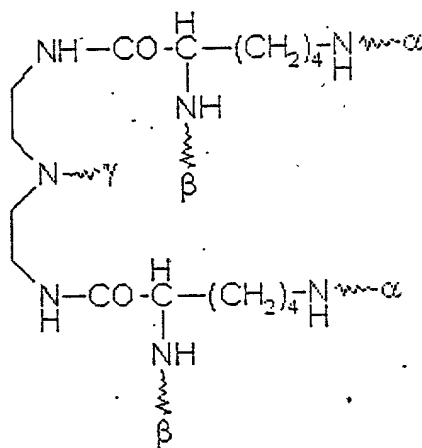
(d)



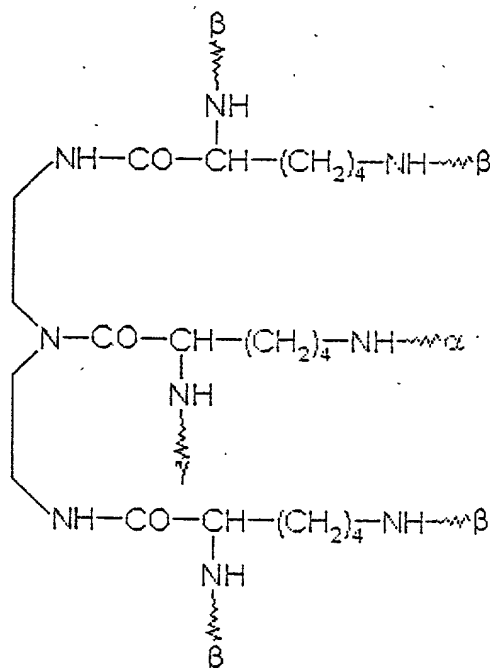
(e)



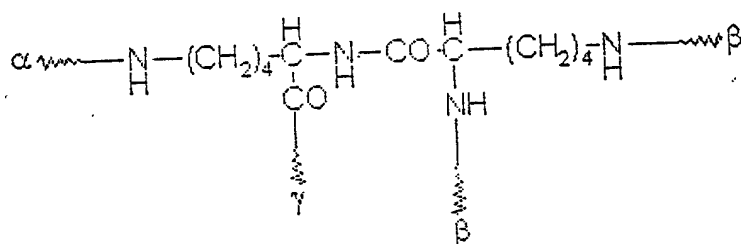
(f)



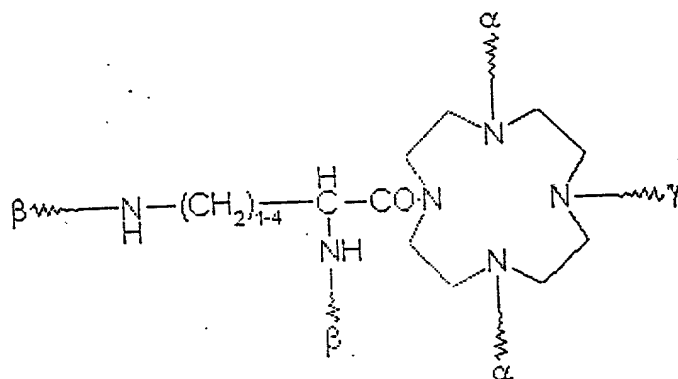
(g)



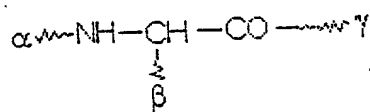
(h)



(i)



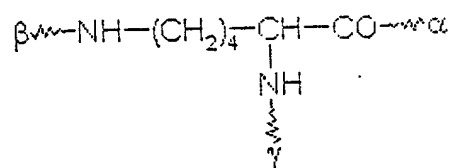
(j)



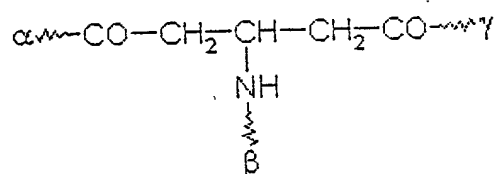
and

G for the case that K means metal complex VIIIc represents a radical that is functionalized in at least three places and is selected from k) or l),

(k)



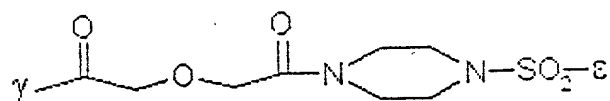
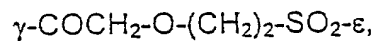
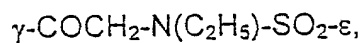
(l)



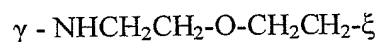
whereby  $\alpha$  means the binding site of G to complex K,  $\beta$  is the binding site of G to radical Y, and  $\gamma$  represents the binding site of G to radical Z,

Y means  $-\text{CH}_2$ ,  $\delta - (\text{CH}_2)_{(1-5)}\text{CO}-\beta$ ,  $\delta - \text{CH}_2 - \text{CHOH} - \text{CO}-\beta$  or  $\delta - \text{CH}(\text{CHOH} - \text{CH}_2\text{OH}) - \text{CHOH} - \text{CHOH} - \text{CO}-\beta$ , whereby  $\delta$  represents the binding site to sugar radical R and  $\beta$  is the binding site to radical G,

Z stands for



or



whereby  $\gamma$  represents the binding site of Z to radical G, and  $\xi$  means the binding site of Z to perfluorinated radical  $\text{R}^{\text{F}}$

and

$l^1, m^1$ , independently of one another, mean integers 1 or 2, and

$p^1$  means integers 1 to 4, are used.

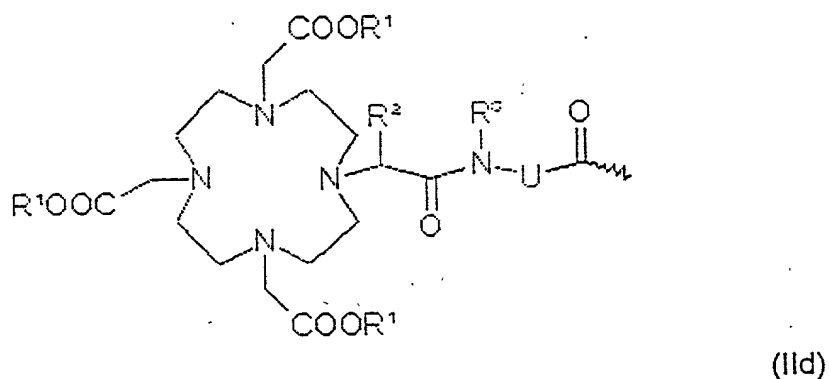
37. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, the compounds with polar radicals of general formula Id



in which

$\text{R}^{\text{F}}$  is a perfluorinated, straight-chain or branched carbon chain with formula  $-\text{C}_n\text{F}_{2n}\text{E}$ , in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

K stands for a metal complex of general formula IId,



in which

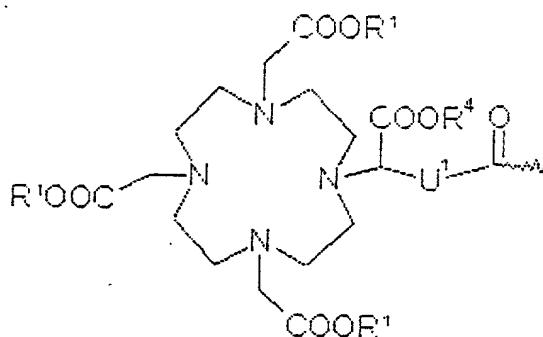
$R^1$  means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two  $R^1$  stand for metal ion equivalents,

$R^2$  and  $R^3$ , independently of one another, represent hydrogen,  $C_1$ - $C_7$  alkyl, benzyl, phenyl,  $-CH_2OH$  or  $-CH_2OCH_3$ , and

U represents  $-C_6H_4-O-CH_2-\omega$ -,  $-(CH_2)_{1.5}-\omega$ , a phenylene group,  $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega$ -,  $-C_6H_4-(OCH_2CH_2)_{0.1}-N(CH_2COOH)-CH_2-\omega$ , or a  $C_1$ - $C_{12}$  alkylene group or  $C_7$ - $C_{12}$ - $C_6H_4-O$  group optionally interrupted by one or more oxygen atoms, 1 to 3  $-NHCO$  groups, 1 to 3  $-CONH$  groups and/or substituted with 1 to 3  $-(CH_2)_{0.5}COOH$  groups, whereby  $\omega$  stands for the binding site to  $-CO-$ ,

or

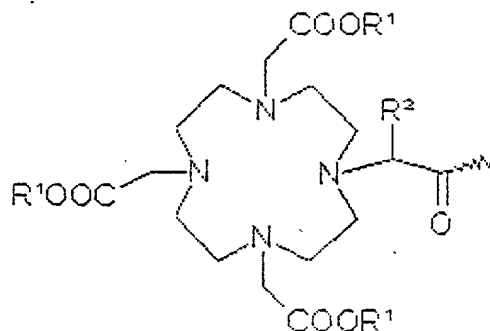
of general formula IIIId



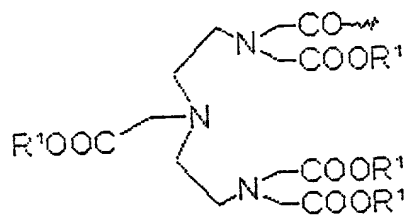
(IIIId)

in which  $R^1$  has the above-mentioned meaning,  $R^4$  represents hydrogen or a metal ion equivalent mentioned under  $R^1$ , and  $U^1$  represents  $-C_6H_4-O-CH_2-\omega$ -, whereby  $\omega$  means the binding site to  $-CO-$ , or

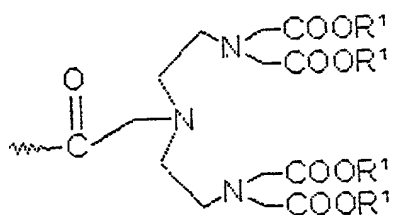
of general formula IVd



in which  $R^1$  and  $R^2$  have the above-mentioned meaning, or of general formula VdA or VdB

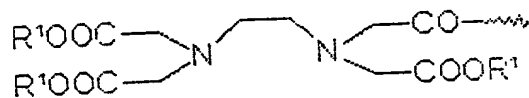


(VdA)



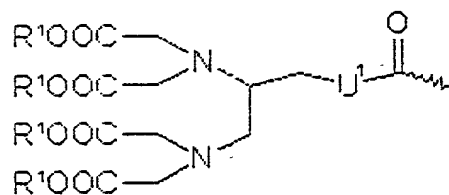
(VdB)

in which  $R^1$  has the above-mentioned meaning, or of general formula VId



(VId)

in which  $R^1$  has the above-mentioned meaning, or of general formula VIId



(VIId)



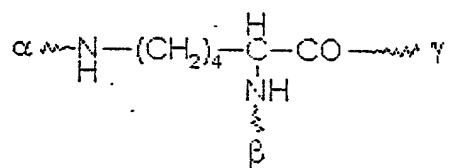
in which  $R^1$  has the above-mentioned meaning, and

$U^1$  represents  $-C_6H_4-O-CH_2-\omega-$ , whereby  $\omega$  means the binding site to  $-CO-$ ,

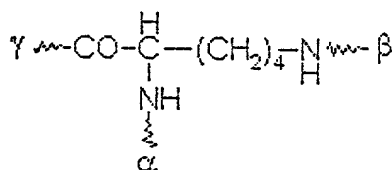
and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

G represents a radical that is functionalized in at least three places and is selected from the following radicals a) to g)

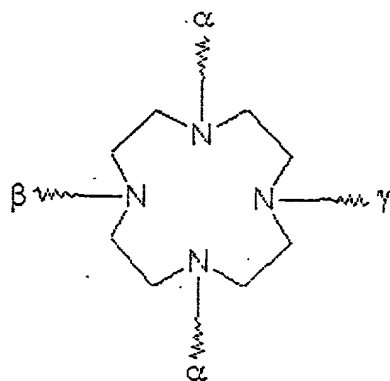
(a)



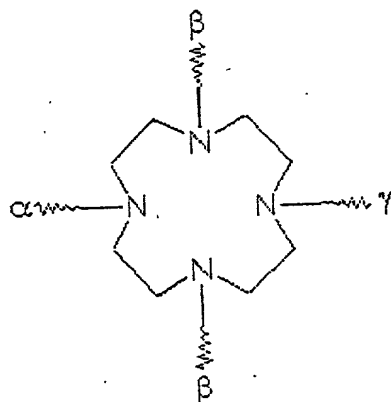
(b)



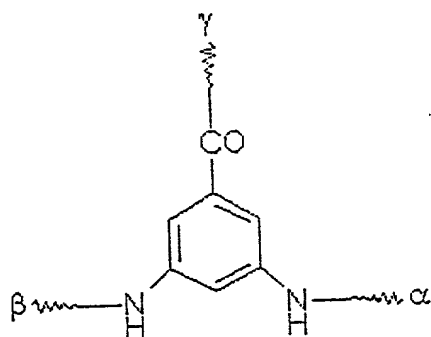
(c)



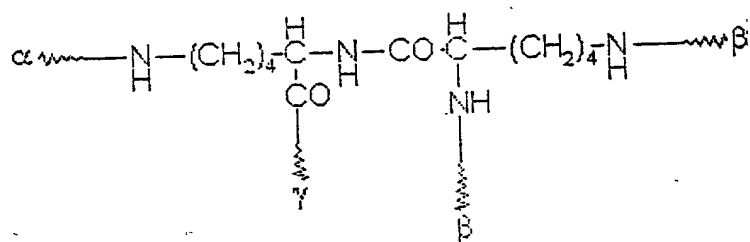
(d)



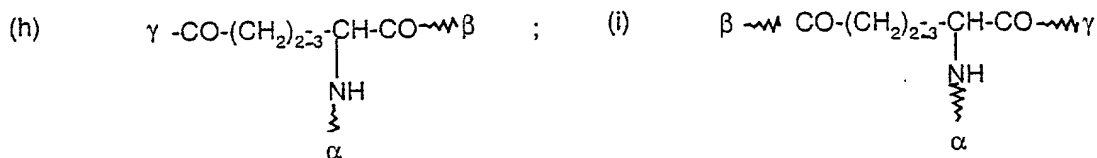
(e)



(f)

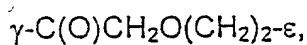


(g)



whereby  $\alpha$  means the binding site of G to complex K,  $\beta$  is the binding site of G to radical R, and  $\gamma$  represents the binding site of G to radical Z

Z stands for



whereby  $\gamma$  represents the binding site of Z to radical G and  $\xi$  means the binding site of Z to perfluorinated radical  $\text{R}_\xi$ ,

R represents a polar radical that is selected from complexes K of general formulas IIId to VIId, whereby  $\text{R}^1$  here means a hydrogen atom or a metal ion equivalent of atomic numbers 20, 23-29, 42-46 or 58-70, and radicals  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ , U and  $\text{U}^1$  have the above-indicated meaning,

or

means the folic acid radical

or

means a carbon chain with 2-30 C atoms that is bonded to radical G via -CO-, or SO<sub>2</sub>- or a direct bond and is straight or branched, saturated or unsaturated,

optionally interrupted by 1-10 oxygen atoms, 1-5 -NHCO groups, 1-5 -CONH groups, 1-2 sulfur atoms, 1-5 -NH groups or 1-2 phenylene groups, which optionally can be substituted with 1-2 OH groups, 1-2 NH<sub>2</sub> groups, 1-2 -COOH groups, or 1-2 -SO<sub>3</sub>H groups,

or

optionally substituted with 1-8 OH groups, 1-5 -COOH groups, 1-2 SO<sub>3</sub>H groups, 1-5 NH<sub>2</sub> groups, 1-5 C<sub>1</sub>-C<sub>4</sub> alkoxy groups, and

l<sup>1</sup>, m<sup>1</sup>, p<sup>2</sup>, independently of one another, mean integers 1 or 2 are used.

44. (Amended) Use according to claim 37, wherein the gadolinium complex of 2,6-N,N'-bis[1,4,7-tris(carboxylatomethyl)-1,4,7,10-tetraazacyclododecane-10-(pentanoyl-3-aza-4-oxo-5-methyl-5-yl)]-lysine-[1-(4-perfluorooctylsulfonyl)-piperazine]-amide is used.


45. (Amended) Use according to claim 1, wherein as perfluoroalkyl-containing metal complexes, galenical formulations that contain paramagnetic, perfluoroalkyl-containing metal complexes of general formulas I, Ia, Ib, Ic and/or Id and diamagnetic perfluoroalkyl-containing substances, preferably dissolved in an aqueous solvent, are used.

REMARKS

The amendments to the application are made to remove the multiple dependency of the claims and to make minor typographical errors. It is respectfully submitted that no new matter has been added and the amendment should be allowed.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Attorney for Applicant(s)

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Attorney Docket No.: SCH-1774

Date: December 18, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

**IN THE CLAIMS:**

Please amend the claims as follows:

3. (Amended) Use according to claim 1 [or 2], wherein the metal complexes are also used as MRI contrast media for visualization of infarcted and necrotic tissue.

4. (Amended) Use according to claim [one of claims] 1 [to 3], wherein the metal complexes are also used as MRI contrast media for independent visualization of necroses and tumors.

8. (Amended) Use according to claim [one of claims] 1 [to 7], wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula I

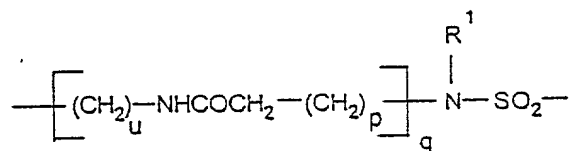


in which

$R^F$  is a perfluorinated, straight-chain or branched carbon chain with formula  $-C_nF_{2n}E$ , in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom and n stands for numbers 4-30,

L means a direct bond, a methylene group, an -NHCO group, a group



[(Please change  $R^1$  to  $R^a$  in the formula!)]

whereby p means the numbers 0 to 10, and q and n, independently of one another, mean numbers 0 or 1, and

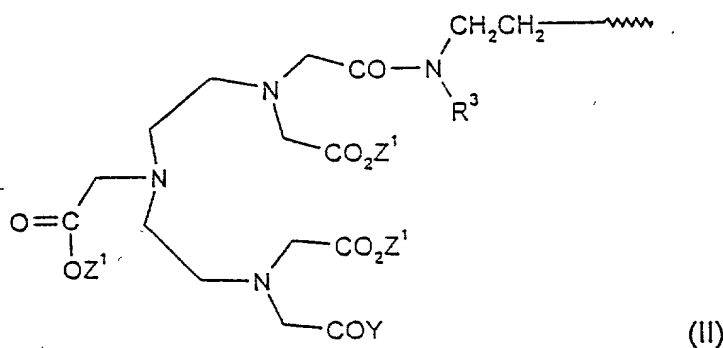
$R^3$  is a hydrogen atom, a methyl group, a  $-\text{CH}_2-\text{OH}$  group, a  $-\text{CH}_2-\text{CO}_2\text{H}$  group or a  $\text{C}_2-\text{C}_{15}$  chain, which optionally is interrupted by 1 to 3 oxygen atoms, 1 to 2  $>\text{CO}$  groups or an optionally substituted aryl group and/or is substituted with 1 to 4 hydroxyl groups, 1 to 2  $\text{C}_1-\text{C}_4$  alkoxy groups, 1 to 2 carboxy groups, a group  $-\text{SO}_3\text{H}-$ ,

or is a straight-chain, branched, saturated or unsaturated  $\text{C}_2-\text{C}_{30}$  carbon chain, which optionally contains 1 to 10 oxygen atoms, 1 to 3  $-\text{NR}^a$  groups, 1 to 2 sulfur atoms, a piperazine, a  $-\text{CONR}^a$  group, an  $-\text{NR}^a\text{CO}$  group, an  $-\text{SO}_2$  group, an  $-\text{NR}^a-\text{CO}_2$  group, 1 to 2  $\text{CO}$  groups, a group  $-\text{CO}-\text{N}-\text{T}-\text{N}(\text{R}^a)-\text{SO}_2-\text{R}^F$ , or 1 to 2 optionally substituted aryls and/or is interrupted by these groups and/or is optionally substituted with 1 to 3  $-\text{OR}^a$  groups, 1 to 2 oxo groups, 1 to 2  $-\text{NH}-\text{COR}^a$  groups, 1 to 2  $-\text{CONHR}^a$  groups, 1 to 2  $-(\text{CH}_2)_p-\text{CO}_2\text{H}$  groups, 1 to 2 groups  $-(\text{CH}_2)_p-(\text{O})_q-\text{CH}_2\text{CH}_2-\text{R}^F$ , whereby

$\text{R}^a$ ,  $\text{R}^F$  and  $p$  and  $q$  have the above-indicated meanings, and

$\text{T}$  means a  $\text{C}_2-\text{C}_{10}$  chain, which optionally is interrupted by 1 to 2 oxygen atoms or 1 to 2  $-\text{NHCO}$  groups,

$\text{K}$  stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides, specifically for a complexing agent or complex of general formula II

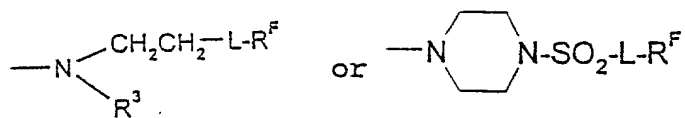


in which  $\text{R}^c$ ,  $\text{R}^1$  and  $\text{B}$  are independent of one another, and

$\text{R}^c$  has the meaning of  $\text{R}^a$  or means  $-(\text{CH}_2)_m-\text{L}-\text{R}^F$ , whereby  $m$  is 0, 1 or 2, and  $\text{L}$  and  $\text{R}^F$  have the above-mentioned meaning,

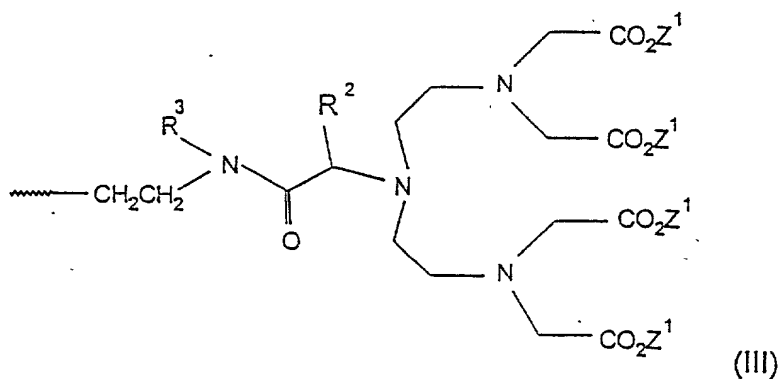
$R^1$ , independently of one another, mean a hydrogen atom or a metal ion equivalent of atomic numbers 22-29, 42-46 or 58-70,

B means  $-OR^1$  or



whereby  $R^1$ , L,  $R^F$  and  $R^c$  have the above-mentioned meanings, or

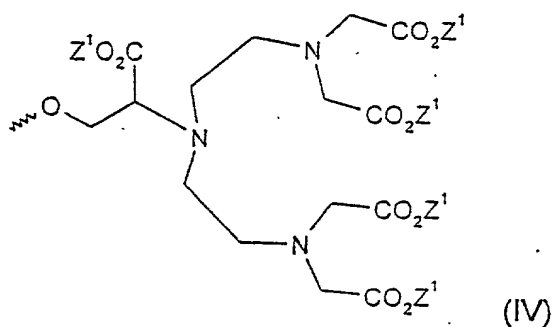
K stands for a complexing agent or complex of general formula III



in which  $R^c$  and  $R^1$  have the above-mentioned meanings and  $R^b$  has the meaning of  $R^a$

or

K stands for a complexing agent or complex of general formula IV

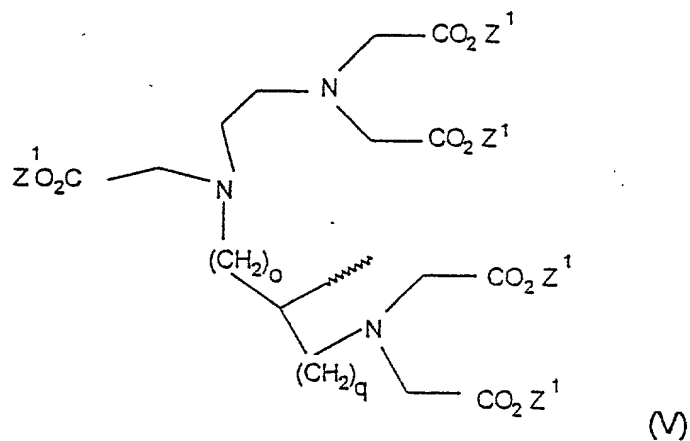




in which  $R^1$  has the above-mentioned meaning

or

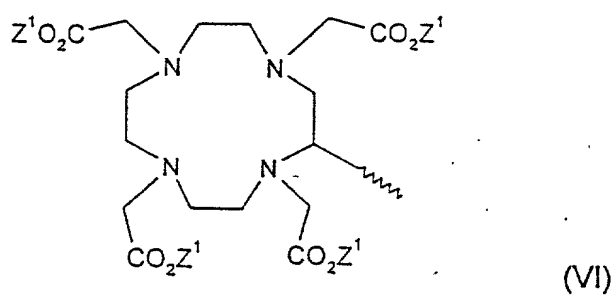
K stands for a complexing agent or complex of general formula V



in which  $R^1$  has the above-mentioned meaning, and o and q stand for numbers 0 or 1, and yields the sum  $o + q = 1$ ,

or

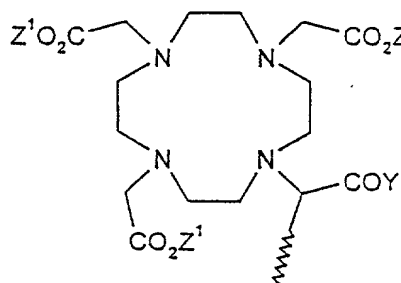
K stands for a complexing agent or complex of general formula VI



in which  $R^1$  has the above-mentioned meaning

or

K stands for a complexing agent or complex of general formula VII

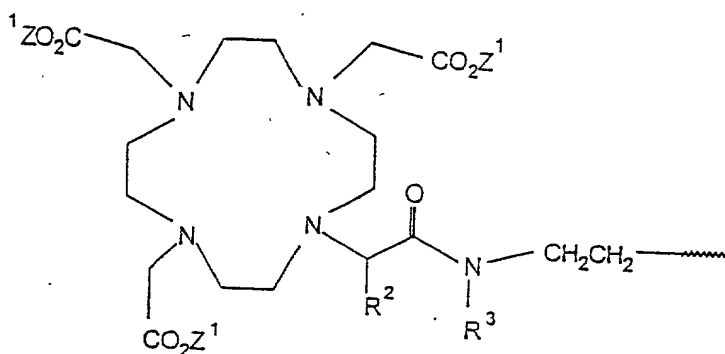


(VII)

in which R<sup>1</sup> and B have the above-mentioned meanings

or

K stands for a complexing agent or complex of general formula VIII

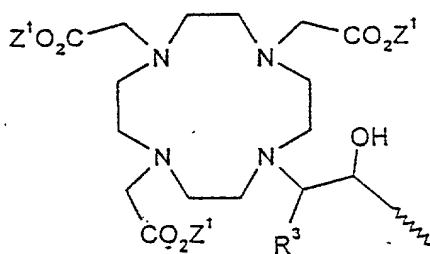


(VIII)

in which R<sup>c</sup> and R<sup>1</sup> have the above-mentioned meanings, and R<sup>b</sup> has the above-mentioned meaning of R<sup>a</sup>

or

K stands for a complexing agent or complex of general formula IX

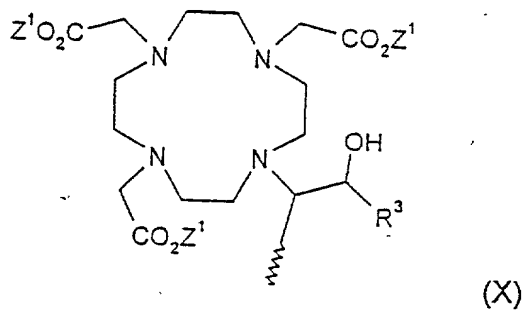


(IX)

in which  $R^c$  and  $R^1$  have the above-mentioned meanings,

or

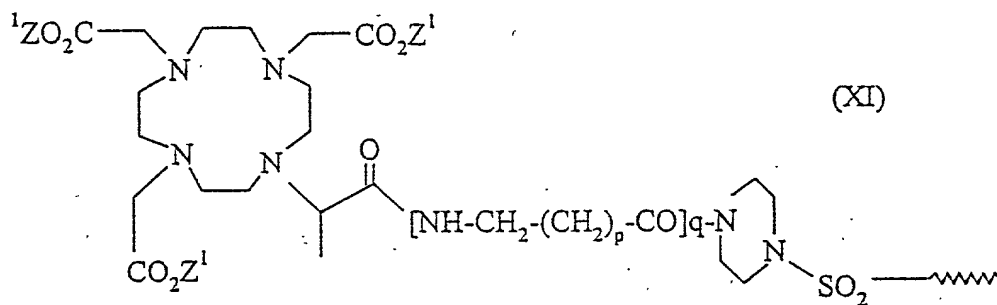
K stands for a complexing agent or complex of general formula X



in which  $R^c$  and  $R^1$  have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XI

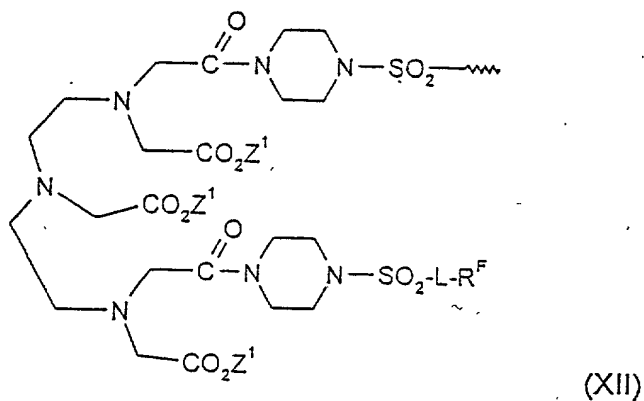


in which  $R^1$ , p and q have the above-mentioned meanings, and  $R^b$  has the meaning of

$R^a$ ,

or

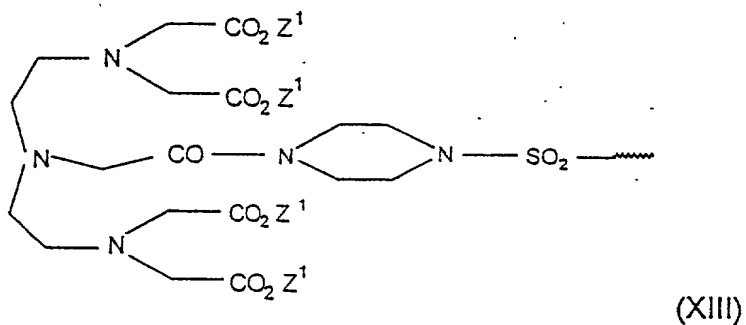
K stands for a complexing agent or complex of general formula XII



in which L, R<sup>F</sup> and Z<sup>1</sup> have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XIII



in which R<sup>1</sup> has the above-mentioned meaning, are used.

10 (Amended) Use according to claim 8 [or 9], wherein the compounds of formula I in which n in formula -C<sub>n</sub>F<sub>2n</sub>E stands for numbers 4-15 and/or E in this formula means a fluorine atom are used.

11. (Amended) Use according to claim [one of claims] 8 [to 10], wherein the following compounds are used:

- Gadolinium complex of 10-[1-methyl-2-oxo-3-aza-5-oxo-{4-perfluorooctylsulfonyl-piperazin-1-yl}-pentyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17-heptadecafluoroheptadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5,9-dioxo-9-{4-perfluorooctyl}-piperazin-1-yl]-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-oxa-1H,1H,2H,3H,3H,5H,5H,6H,6H-perfluorotetradecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,-16,16,17,17,18,18,19,19-henicosafuoro-nonadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-11-aza-11-(perfluorooctylsulfonyl)-tridecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,
- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-8-phenyl-octyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane.

12. (Amended) Use according to claim [one of claims] 1[-7], wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ia

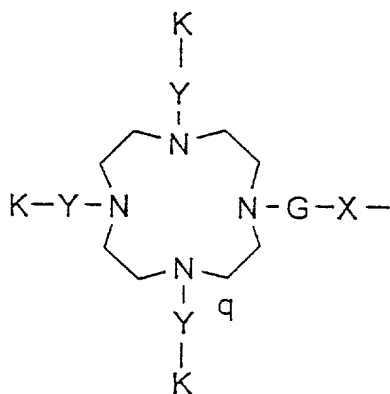


in which

- A is a molecule part that contains 2 to 6 metal complexes, which are bonded directly or via a linker to a nitrogen atom of an annular skeleton chain, and
- $R^F$  is a perfluorinated, straight-chain or branched carbon chain with formula -  $C_nF_{2n}E$ , in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

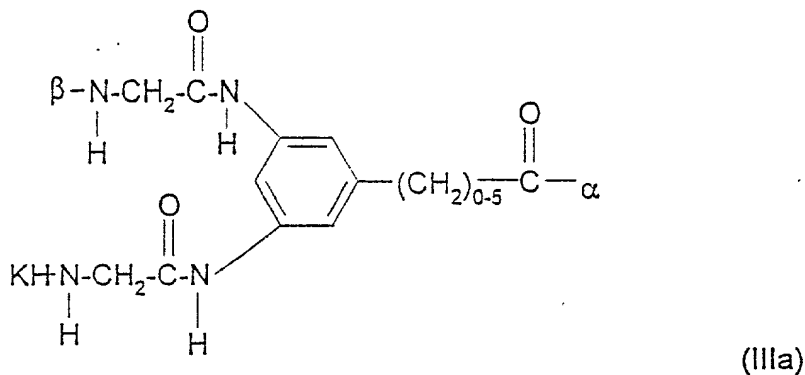
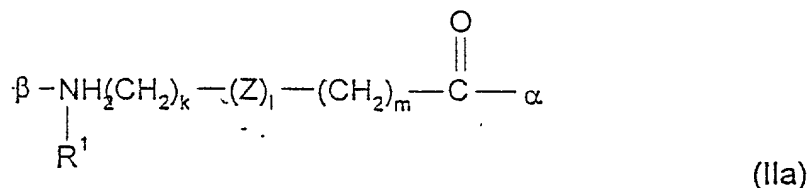
whereby molecule part A has the following structure:



whereby

- $q^1$  is a number 0, 1, 2 or 3,
- K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides,
- X is a direct bond to the perfluoroalkyl group, a phenylene group or a  $C_1$ - $C_{10}$  alkylene chain, which optionally contains 1-15 oxygen atoms, 1-5 sulfur atoms, 1-10 carbonyl groups, 10-10 ( $NR^d$ ) groups, 1-2  $NR^dSO_2$  groups, 1-10  $CONR^d$  groups, 1 piperidine group, 1-3  $SO_2$  groups and 1-2 phenylene groups or optionally is substituted by 1-3 radicals  $R^F$ , in which  $R^d$  stands for a hydrogen atom, a phenyl group, benzyl group or a  $C_1$ - $C_{15}$  alkyl group, which optionally contains 1-2  $NHCO$ , 1-2  $CO$  groups, 1-5 oxygen atoms and optionally is substituted by 1-5 Hydroxy, 1-5 methoxy, 1-3 carboxy, or 1-3  $R^F$  radicals,

- V is a direct bond or a chain of general formula IIa or IIIa:



in which

- $R^e$  is a hydrogen atom, a phenyl group, a benzyl group or a  $C_1$ - $C_7$  alkyl group, which optionally is substituted with a carboxy group, a methoxy group or a hydroxy group,
- W is a direct bond, a polyglycol ether group with up to 5 glycol units, or a molecule part of general formula IVa



in which  $R^h$  is a  $C_1$ - $C_7$  carboxylic acid, a phenyl group, a benzyl group or a  $-(CH_2)_{1-5}$ -NH-K group,

- $\alpha$  represents the binding to the nitrogen atom of the skeleton chain,  $\beta$  represents the binding to complexing agents or metal complex K,
- and in which variables k and m stand for natural numbers between 0 and 10, and l stands for 0 or 1

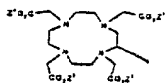
and whereby

- D is a CO or  $SO_2$  group, are used.

20. (Amended) Use according to claim [one of claims] 12 [to 19], wherein the compounds of general formula Ia in which the perfluoroalkyl chain is  $R^F$ -C<sub>6</sub>F<sub>13</sub>, -C<sub>8</sub>F<sub>17</sub>, -C<sub>10</sub>F<sub>21</sub> or -C<sub>12</sub>F<sub>25</sub> are used.

21. (Amended) Use according to claim [one of claims] 12 [to 20], wherein the gadolinium complex of 1,4,7-tris{1,4,7-tris(N-(carboxylatomethyl)-10-[N-1-methyl-3,6-diaza-2,5,8-trioxooctane-1,8-diyl])-1,4,7,10-tetraazacyclododecane, Gd complex}-10-[N-2H,2H,4H,4H,5H,5H-3-oxa-perfluorotridecanoyl]-1,4,7,10-tetraazacyclododecane is used.

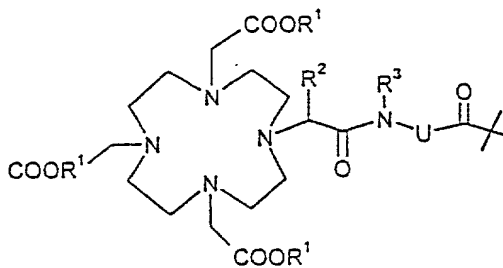
22. (Amended) Use according to claim [one of claims] 1 [to 7], wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ib



(Ib)

in which

K means a complexing agent or a metal complex of general formula IIb



(IIb)



whereby

R<sup>1</sup> stands for a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70,

R<sup>2</sup> and R<sup>3</sup> stand for a hydrogen atom, a C<sub>1</sub>-C<sub>7</sub> alkyl group, a benzyl group, a phenyl group, -CH<sub>2</sub>OH or -CH<sub>2</sub>-OCH<sub>3</sub>,

U<sup>2</sup> stands for radical L<sup>1</sup>, whereby L<sup>1</sup> and U<sup>2</sup>, independently of one another, can be the same or different,

A<sup>1</sup> means a hydrogen atom, a straight-chain or branched C<sub>1</sub>-C<sub>30</sub> alkyl group, which optionally is interrupted by 1-15 oxygen atoms, and/or optionally is substituted with 1-10 hydroxy groups, 1-2 COOH groups, a phenyl group, a benzyl group and/or 1-5 -OR<sup>9</sup> groups, with R<sup>9</sup> in the meaning of a hydrogen atom or a C<sub>1</sub>-C<sub>7</sub> alkyl radical, or -L<sup>1</sup>-R<sup>F</sup>,

L<sup>1</sup> means a straight-chain or branched C<sub>1</sub>-C<sub>30</sub> alkylene group, which optionally is interrupted by 1-10 oxygen atoms, 1-5 -NH-CO groups, 1-5 -CO-NH groups, by a phenylene group optionally substituted by a COOH- group, 1-3 sulfur atoms, 1-2 -N(B<sup>1</sup>)-SO<sub>2</sub> groups and/or 1-2 -SO<sub>2</sub>-N(B<sup>1</sup>)-groups with B<sup>1</sup> in the meaning of A<sup>1</sup>, an NHCO group, a CONH group, an N(B<sup>1</sup>)-SO<sub>2</sub> group or an -SO<sub>2</sub>-N(B<sup>1</sup>) group and/or optionally is substituted with radical R<sup>F</sup>, and

R<sup>F</sup> means a straight-chain or branched perfluorinated alkyl radical of formula C<sub>n</sub>F<sub>2n</sub>E, whereby n stands for number 4-30, and

E stands for a terminal fluorine atom, chlorine atom, bromine atom, iodine atom or a hydrogen atom,

and optionally present acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides, are used.

29. (Amended) Use according to claim [one of claims] 22 [to 28], wherein the following compounds are used:

-- 1,4,7-Tris(carboxylatomethyl)-10-(3-aza-4-oxo-hexan-5-yl)-acid-(2,3-dihydroxypropyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl)-amide]-

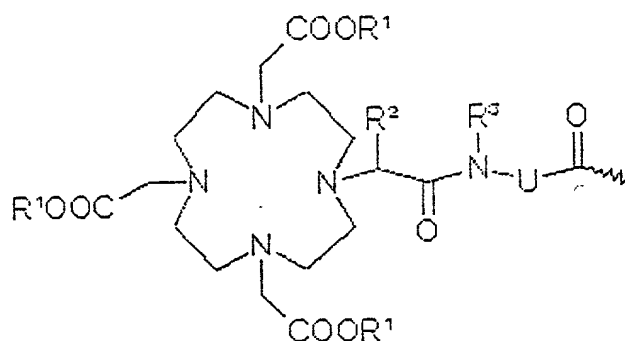
- 1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-{(3-aza-4-oxo-hexan-5-yl)ic)acid-N-(3,6,9,12,15-pentaoxa)-hexadecyl)-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-{(3-aza-4-oxo-hexan-5-yl)ic)-acid-N-5-hydroxy-3-oxa-pentyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-{(3-aza-4-oxo-hexan-5-yl)ic)-acid-[N-3,6,9,15-tetraoxa-12-aza-15-oxo-C<sub>17</sub>-C<sub>26</sub>-hepta-decafluor)hexacosyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex
- 1,4,7-Tris(carboxylatomethyl)-10-[(3-aza-4-oxo-hexan-5-yl)ic)-acid-N-(2-methoxyethyl)-N-(1H,1H,2H,2H,4H,4H,5H,5H-3-oxa)-perfluorotridecyl]-amide}-1,4,7,10-tetraazacyclododecane, gadolinium complex.

30. (Amended) Use according to claim [one of claims] 1 [to 7], wherein as perfluoroalkyl-containing metal complexes, the compounds with sugar radicals of general formula Ic



in which

- R represents a mono-or oligosaccharide radical bonded by the 1-OH- or 1-SH-position,
- R<sup>F</sup> is a perfluorinated, straight-chain or branched carbon chain with the formula -C<sub>n</sub>F<sub>2n</sub>E, in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,
- K stands for a metal complex of general formula IIc,



(IIc)

in which

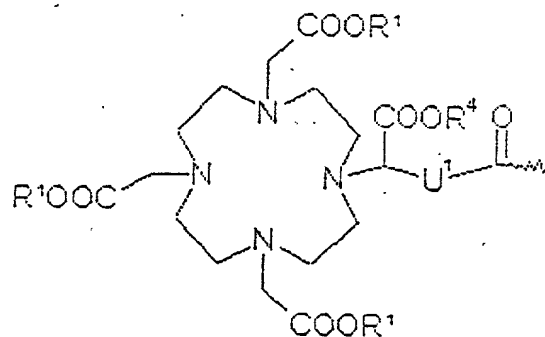
$R^1$  means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two  $R^1$  stand for metal ion equivalents,

$R^2$  and  $R^3$ , independently of one another, represent hydrogen,  $C_1$ - $C_7$  alkyl, benzyl, phenyl,  $-CH_2OH$  or  $-CH_2OCH_3$ , and

$U$  represents  $-C_6H_4-O-CH_2-\omega$ ,  $-(CH_2)_{1-5}-\omega$ , a phenylene group,  $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega$ ,  $-C_6H_4-(OCH_2CH_2)_{0-1}-N(CH_2COOH)-CH_2-\omega$ , or a  $C_1$ - $C_{12}$  alkylene group or  $C_7$ - $C_{12}$ - $C_6H_4-O$  group optionally interrupted by one or more oxygen atoms, 1 to 3  $-NHCO$  groups or 1 to 3  $-CONH$  groups and/or substituted with 1 to 3  $-(CH_2)_{0-5} COOH$  groups, whereby  $\omega$  stands for the binding site to  $-CO-$ ,

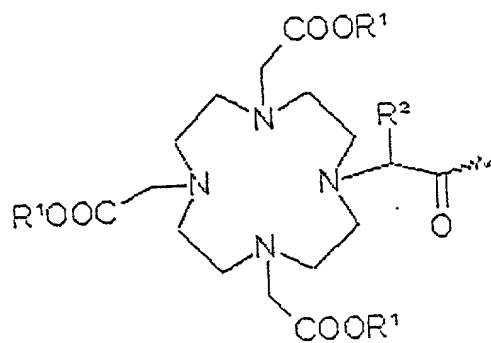
or

of general formula IIIc



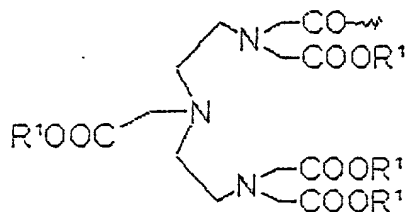
(IIIc)

in which  $R^1$  has the above-mentioned meaning,  $R^4$  represents hydrogen or a metal ion equivalent mentioned under  $R^1$ , and  $U^1$  represents  $-C_6H_4-O-CH_2-\omega$ , whereby  $\omega$  means the binding site to  $-CO-$ , or of general formula IVc

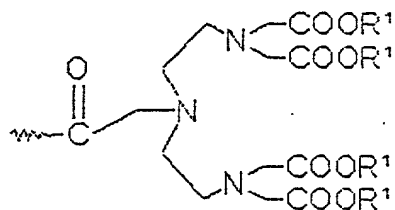


(IVc)

in which  $R^1$  and  $R^2$  have the above-mentioned meaning or of general formula VcA or VcB



(VcA)



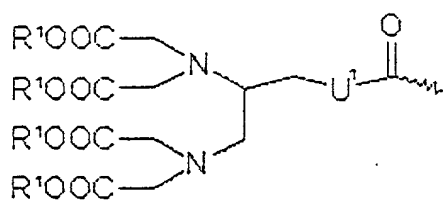
(VcB)

in which  $R^1$  has the above-mentioned meaning, or of general formula VIc



(VIc)

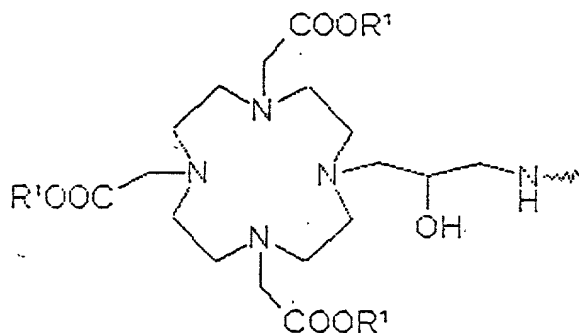
in which  $R^1$  has the above-mentioned meaning, or of general formula VIIc



(VIIc)

in which  $R^1$  has the above-mentioned meaning, and

$U^1$  represents  $-C_6H_4-O-CH_2-\omega$ , whereby  $\omega$  means the binding site to  $-CO-$  or of general formula VIIIc

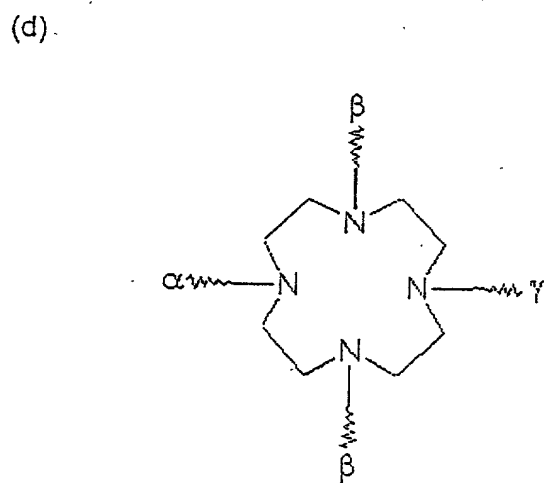
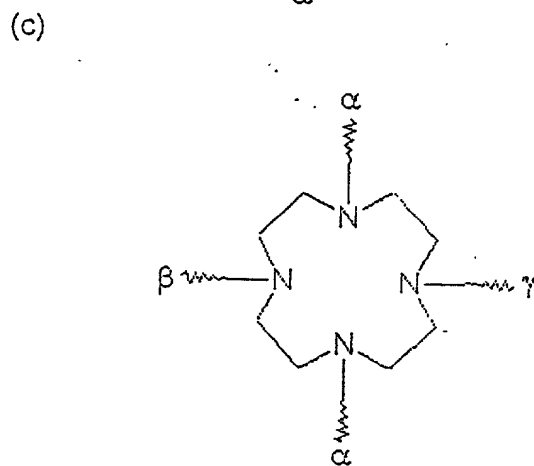
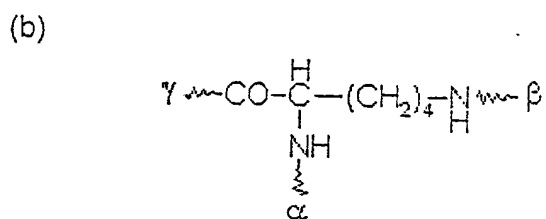
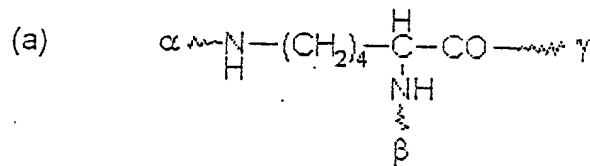


(VIIIc)

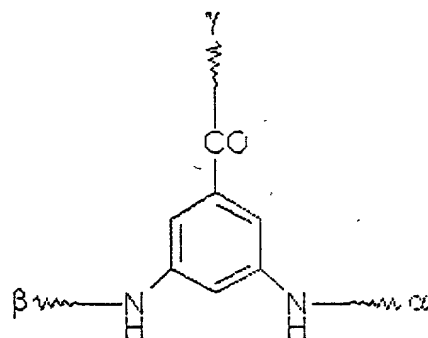
in which  $R^1$  has the above-mentioned meaning,

and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

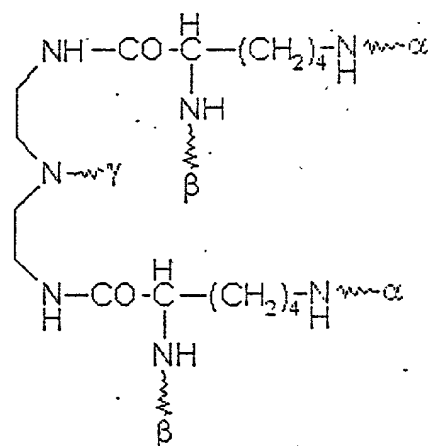
- G for the case that K means metal complexes IIc to VIIc represents a radical that is functionalized in at least three places and is selected from the following radicals a) to j)



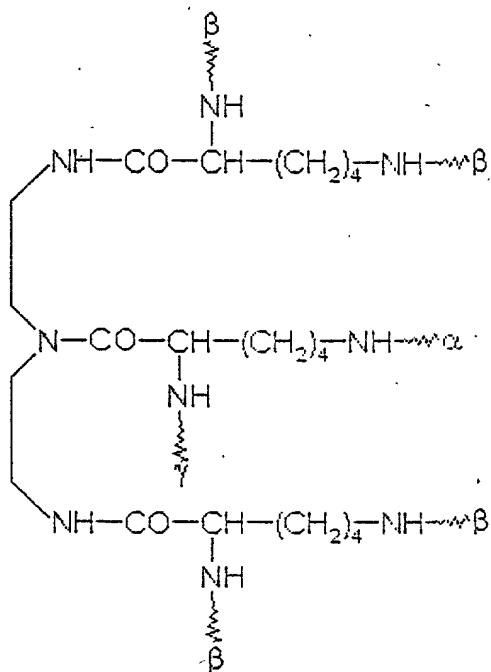
(e)



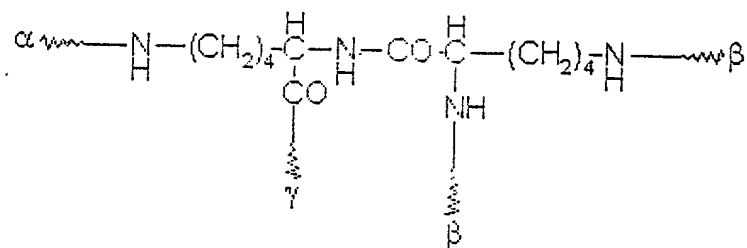
(f)



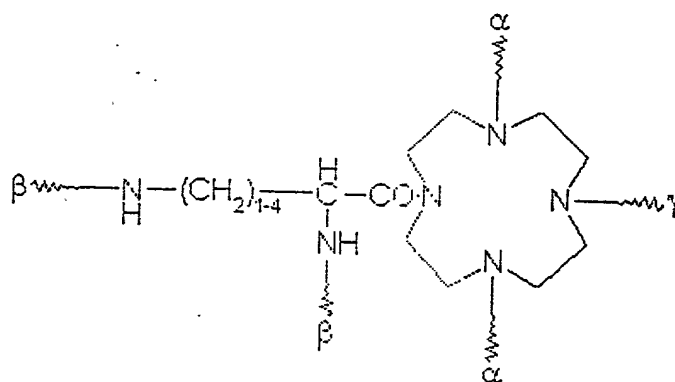
(g)



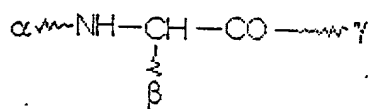
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(i)



(i)

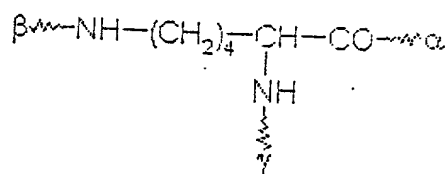


and

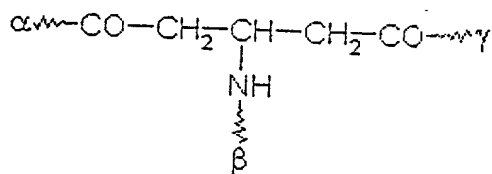
G for the case that K means metal complex VIIIc represents a radical that is functionalized in at least three places and is selected from k) or l),



(k)



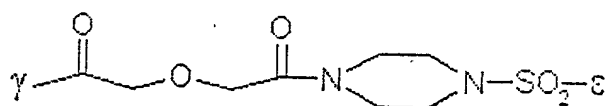
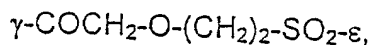
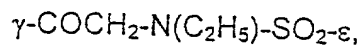
(l)



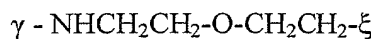
whereby  $\alpha$  means the binding site of G to complex K,  $\beta$  is the binding site of G to radical Y, and  $\gamma$  represents the binding site of G to radical Z,

Y means  $-\text{CH}_2$ ,  $\delta - (\text{CH}_2)_{(1-5)}\text{CO}-\beta$ ,  $\delta - \text{CH}_2 - \text{CHOH} - \text{CO}-\beta$  or  $\delta - \text{CH}(\text{CHOH} - \text{CH}_2\text{OH}) - \text{CHOH} - \text{CHOH} - \text{CO}-\beta$ , whereby  $\delta$  represents the binding site to sugar radical R and  $\beta$  is the binding site to radical G,

Z stands for



or



whereby  $\gamma$  represents the binding site of Z to radical G, and  $\xi$  means the binding site of Z to perfluorinated radical  $\text{R}^{\text{F}}$

and

$l^1$ ,  $m^1$ , independently of one another, mean integers 1 or 2, and

$p^1$  means integers 1 to 4, are used.

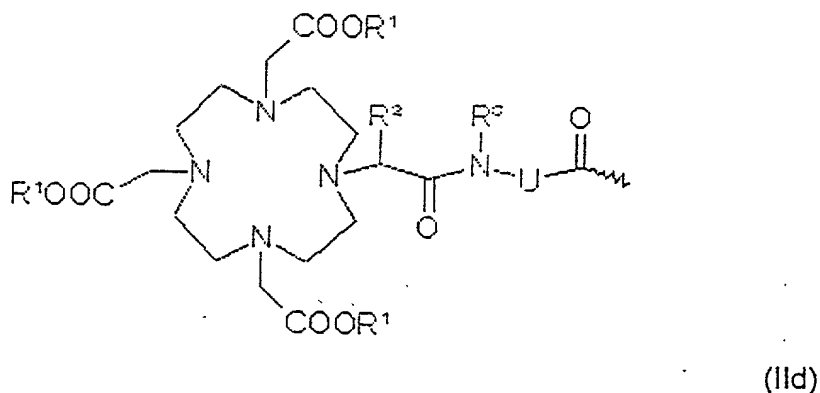
37. (Amended) Use according to claim [one of claims] 1 [to 7], wherein as perfluoroalkyl-containing metal complexes, the compounds with polar radicals of general formula Id



in which

$\text{R}^{\text{F}}$  is a perfluorinated, straight-chain or branched carbon chain with formula  $\text{-C}_n\text{F}_{2n}\text{E}$ , in which E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom, and n stands for numbers 4-30,

K stands for a metal complex of general formula IIId,



in which

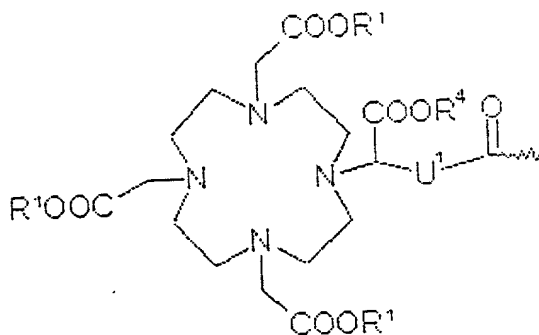
$R^1$  means a hydrogen atom or a metal ion equivalent of atomic numbers 23-29, 42-46 or 58-70, provided that at least two  $R^1$  stand for metal ion equivalents,

$R^2$  and  $R^3$ , independently of one another, represent hydrogen,  $C_1$ - $C_7$  alkyl, benzyl, phenyl,  $-CH_2OH$  or  $-CH_2OCH_3$ , and

U represents  $-C_6H_4-O-CH_2-\omega-$ ,  $-(CH_2)_{1-5}-\omega$ , a phenylene group,  $-CH_2-NHCO-CH_2-CH(CH_2COOH)-C_6H_4-\omega-$ ,  $-C_6H_4-(OCH_2CH_2)_{0-1}-N(CH_2COOH)-CH_2-\omega$ , or a  $C_1$ - $C_{12}$  alkylene group or  $C_7$ - $C_{12}$ - $C_6H_4-O$  group optionally interrupted by one or more oxygen atoms, 1 to 3  $-NHCO$  groups, 1 to 3  $-CONH$  groups and/or substituted with 1 to 3  $-(CH_2)_{0-5}COOH$  groups, whereby  $\omega$  stands for the binding site to  $-CO-$ ,

or

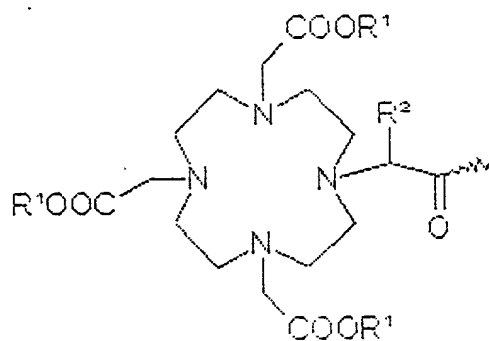
of general formula IIIId



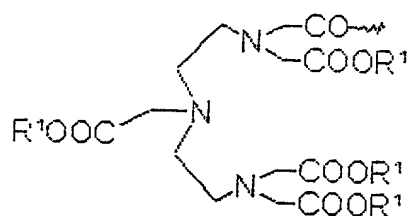
(IIIId)

in which  $R^1$  has the above-mentioned meaning,  $R^4$  represents hydrogen or a metal ion equivalent mentioned under  $R^1$ , and  $U^1$  represents  $-C_6H_4-O-CH_2-\omega-$ , whereby  $\omega$  means the binding site to  $-CO-$ , or

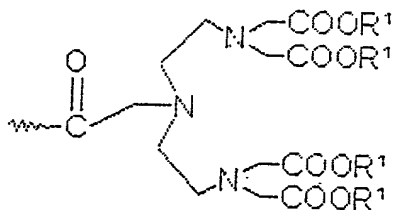
of general formula IVd



in which R<sup>1</sup> and R<sup>2</sup> have the above-mentioned meaning, or of general formula VdA or VdB



(VdA)



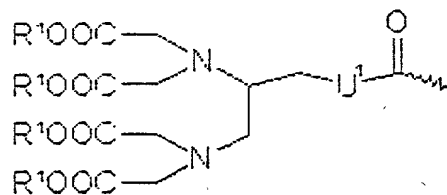
(VdB)

in which R<sup>1</sup> has the above-mentioned meaning, or of general formula VId



(VId)

in which R<sup>1</sup> has the above-mentioned meaning, or of general formula VIId



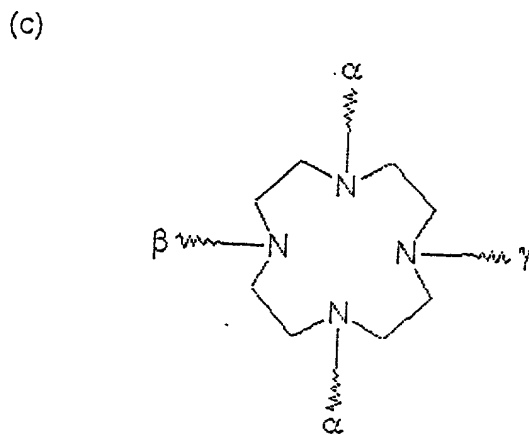
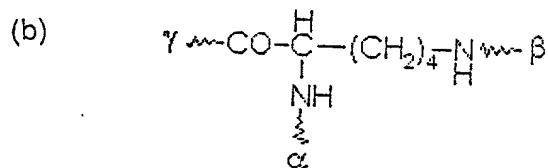
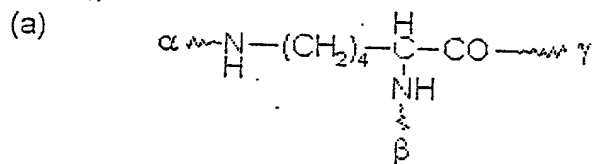
(VIId)

in which R<sup>1</sup> has the above-mentioned meaning, and

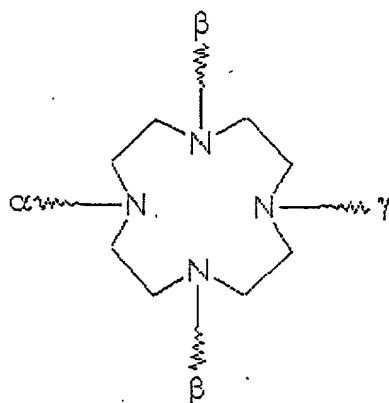
U<sup>1</sup> represents -C<sub>6</sub>H<sub>4</sub>-O-CH<sub>2</sub>-ω-, whereby ω means the binding site to -CO-,

and in radical K, optionally present free acid groups optionally can be present as salts of organic and/or inorganic bases or amino acids or amino acid amides,

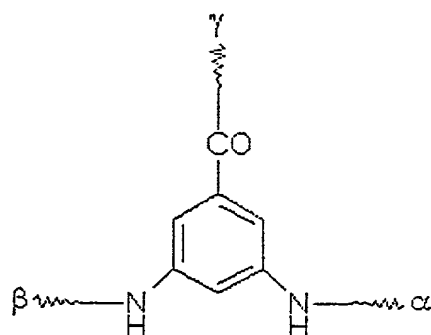
G represents a radical that is functionalized in at least three places and is selected from the following radicals a) to g)



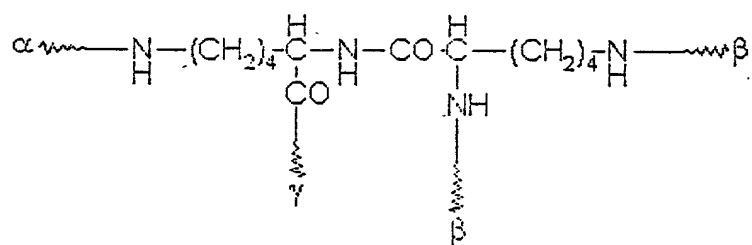
(d)



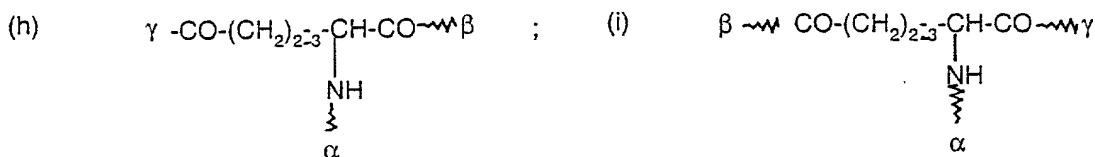
(e)



(f)

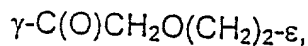


(g)



whereby  $\alpha$  means the binding site of G to complex K,  $\beta$  is the binding site of G to radical R, and  $\gamma$  represents the binding site of G to radical Z

Z stands for



whereby  $\gamma$  represents the binding site of Z to radical G and  $\xi$  means the binding site of Z to perfluorinated radical  $\text{R}_f$ ,

R represents a polar radical that is selected from complexes K of general formulas IIId to VIId, whereby  $\text{R}^1$  here means a hydrogen atom or a metal ion equivalent of atomic numbers 20, 23-29, 42-46 or 58-70, and radicals  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ , U and  $\text{U}^1$  have the above-indicated meaning,

or

means the folic acid radical

or

means a carbon chain with 2-30 C atoms that is bonded to radical G via -CO-, or SO<sub>2</sub>- or a direct bond and is straight or branched, saturated or unsaturated,

optionally interrupted by 1-10 oxygen atoms, 1-5 -NHCO groups, 1-5 -CONH groups, 1-2 sulfur atoms, 1-5 -NH groups or 1-2 phenylene groups, which optionally can be substituted with 1-2 OH groups, 1-2 NH<sub>2</sub> groups, 1-2 -COOH groups, or 1-2 -SO<sub>3</sub>H groups,

or

optionally substituted with 1-8 OH groups, 1-5 -COOH groups, 1-2 SO<sub>3</sub>H groups, 1-5 NH<sub>2</sub> groups, 1-5 C<sub>1</sub>-C<sub>4</sub> alkoxy groups, and

l<sup>1</sup>, m<sup>1</sup>, p<sup>2</sup>, independently of one another, mean integers 1 or 2 are used.

44. (Amended) Use according to claim [one of claims] 37[-43], wherein the gadolinium complex of 2,6-N,N'-bis[1,4,7-tris(carboxylatomethyl)-1,4,7,10-tetraazacyclododecane-10-(pentanoyl-3-aza-4-oxo-5-methyl-5-yl)]-lysine-[1-(4-perfluorooctylsulfonyl)-piperazine]-amide is used.

45. (Amended) Use according to claim [one of claims] 1[-7], wherein as perfluoroalkyl-containing metal complexes, galenical formulations that contain paramagnetic, perfluoroalkyl-containing metal complexes of general formulas I, Ia, Ib, Ic and/or Id and diamagnetic perfluoroalkyl-containing substances, preferably dissolved in an aqueous solvent, are used.